

METHOD OF SCREENING FOR AGENTS INHIBITING CHLORIDE
INTRACELLULAR CHANNELS

ABSTRACT OF THE DISCLOSURE

5 [00121] The present invention isolates and characterizes the *exc-4* gene of *C. elegans*,
and identifies *exc-4* as an orthologue of the human CLIC family of chloride intracellular
channels. Accordingly, a nucleic acid having the sequence of SEQ ID NO.: 1 is disclosed, as
well as recombinant vectors and host cells comprising the nucleic acid sequence of SEQ ID
NO.: 1. Further, a number of screening methods are disclosed to identify putative agents that
10 inhibit vertebrate, and preferably human, CLICs using *C. elegans* and *exc-4* inhibition as a
loss-of-function model for CLIC activity. Also disclosed is a method of determining whether
a specific member of the CLIC gene family is involved in tubulogenesis, where the rescue of
a *C. elegans exc-4* excretory cell phenotype *via* expression of a transgenic CLIC gene of
interest indicates that the CLIC gene of interest is involved in tubulogenesis. Finally, a
15 method is disclosed of identifying putative vertebrate, and preferably human, CLIC inhibitors
using transgenic *C. elegans exc-4* mutant embryos, where expression of the transgene yields a
CLIC product that rescues the *exc-4* mutant phenotype. Agents of interest resulting in a
reversionary *exc-4* mutant phenotype are putative agents that inhibit CLIC expression or
function.